APPENDIX A

1. A composition comprising a mocarhagin protein at least 95% free of other cobra proteins.

2. The composition of claim 1 wherein said mocarhagin protein is full-length mocarhagin.

3. The composition of claim 1 wherein said mocarhagin protein is a fragment of full-length mocarhagin having mocarhagin proteolytic activity.

4. The composition of claim 1 wherein said mocarhagin protein exhibits an IC_{50} of less than about 100 μg/mL in a neutrophil/HL60 binding inhibition assay.

5. The composition of claim 1 wherein said mocarhagin protein is characterized by at least one characteristic selected from the group consisting of:

(a) a molecular weight of approximately 55 kDa under reducing conditions;

(b) a molecular weight of approximately 55 kDa under nonreducing conditions;

(c) an N-terminal amino acid sequence comprising

TNTPEQDRYLQAKKYIEFYVVVDNVMYRKY (SEQ NO 1);

(d) mocarhagin proteolytic activity;

(e) the ability to inhibit platelet binding to vWF;

(f) requirement of calcium ion for activity;

(g) requirement of zinc ion for activity

(h) an activity substantially inhibited by excess EDTA; and

(i) an activity substantially inhibited by high concentrations of DFP.

6. The composition of claim 1 wherein said mocarhagin protein is capable of cleaving a material selected from the group consisting of anionic polypeptides containing sulfated tryosine residues, PSGL-1 and GP1bα.

7. A composition comprising a therapeutically effective amount of a composition of claim 1 and a pharmaceutically acceptable carrier.

8. A method of treating an inflammatory disease comprising administering a therapeutically effective amount of a composition of claim 7 to a mammalian subject.

9. A method of inhibiting selecting-mediated binding comprising administering a therapeutically effective amount of a composition of claim 7 to a mammalian subject.

10. A method of isolating mocarhagin from venom, said method comprising:

(a) subjecting a composition comprising cobra venom to a heparin affinity chromatography column;

(b) subjecting the elute from said heparin affinity column to a size exclusion column;

(c) subjecting the eluate from said size exclusion column to a Mono S column; and

(d) eluting said mocarhagin from said Mono S column.

11. A composition comprising a protein isolated according to the method of claim 10.

12. The composition of claim 11 further comprising a pharmaceutically acceptable carrier.

13. A method of treating an inflammatory disease comprising administering a therapeutically effective amount of a composition of claim 12 to a mammalian subject.

14. A method of inhibiting selectin-mediated binding comprising administering a therapeutically effective amount of a composition of claim 12 to a mammalian subject.

15. A composition comprising an antibody which specifically reacts with the mocarhagin of the composition of claim 1 or a fragment thereof having mocarhagin proteolytic activity.

16. The composition of claim 4 wherein said mocarhagin protein exhibits of IC_{50} of less than about 1 μg/mL in a neutrophil/HL60 binding inhibition assay.

17. The composition of claim 1 wherein said mocarhagin protein is homogeneous.

18. The composition of claim 1 wherein the N-terminal sequence of said protein is

TNTPEQDRYLQAKKYIEFYVVVDNVMYRKYTGKLHVITXXVYEMNALN (SEQ ID NO: 2).

19. The composition of claim 5 wherein said protein comprises the amino acid sequence of SEQ ID NO: 6 from amino acid 192 to amino acid 621.

20. A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 6;

(b) the amino acid sequence of SEQ ID NO: 6 from amino acid 24 to amino acid 621;

(c) the amino acid sequence of SEQ ID NO:6 from amino acid 192 to amino acid 621;

(d) fragments of the amino acid sequence of SEQ ID NO: 6 encoding a protein having mocarhagin activity; and

(e) the amino acid sequence encoded by the cDNA insert of clone NMM-1 deposited under accession number ATCC 209588;

the protein being substantially free from other mammalian proteins.

21. The composition of claim 20 wherein said protein comprises the amino acid sequence of SEQ ID NO: 6.

27. A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:5 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

28. The protein of claim 27 comprising a mature protein.

29. A pharmaceutical composition comprising a protein of claim 20 and a pharmaceutically acceptable carrier.

30. A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:8;

(b) the amino acid sequence of SEQ ID NO:8 from amino acid 24 to amino acid 439;

(c) the amino acid sequence of SEQ ID NO: 8 from amino acid 192 to amino acid 439;

(d) fragments of the amino acid sequence of SEQ ID NO:8 encoding a protein having mocarhagin activity; and

(e) the amino acid sequence encoded by the cDNA insert of clone NMM-2 deposited under accession number ATCC 209589;

the protein being substantially free from other mammalian proteins.

31. The composition of claim 30 wherein said protein comprises the amino acid sequence of SEQ ID NO: 6.

37. A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

38. The protein of claim 37 comprising a mature protein.

39. A pharmaceutical composition comprising a protein of claim 30 and a pharmaceutically acceptable carrier.

40. A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 10;

(b) the amino acid sequence of SEQ ID NO: 10 from amino acid 24 to amino acid 613;

(c) the amino acid sequence of SEQ ID NO: 10 from amino acid 192 to amino acid 613;

(d) fragments of the amino acid sequence of SEQ ID NO:10 encoding a protein having mocarhagin activity; and

(e) the amino acid sequence encoded by the cDNA insert of clone NMM-9 deposited under accession number ATCC 209586;

the protein being substantially free from other mammalian proteins.

41. The composition of claim 40 wherein said protein comprises the amino acid sequence of SEQ ID NO:6.

47. A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

48. The protein of claim 47 comprising a mature protein.

49. A pharmaceutical composition comprising a protein of claim 40 and a pharmaceutically acceptable carrier.

50. A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 12;

(b) the amino acid sequence of SEQ ID NO: 12 from the amino acid 24 to amino acid 521;

(c) the amino acid sequence of SEQ ID NO:12 from amino acid 192 to amino acid 521;

(d) fragments of the amino acid sequence of SEQ ID NO:12 encoding a protein having mocarhagin activity; and

(e) the amino acid sequence encoded by the cDNA insert of clone NMM-12 deposited under accession number ATCC 209585;

the protein being substantially free from other mammalian proteins.

51. The composition of claim 50 wherein said protein comprises the amino acid sequence of SEQ ID NO:6.

57. A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

58. The protein of claim 57 comprising a mature protein.

59. A pharmaceutical composition comprising a protein of claim 50 and a pharmaceutically acceptable carrier.

60. A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:14;

(b) the amino acid sequence of SEQ ID NO: 14 from amino acid 24 to amino acid 592;

(c) the amino acid sequence of SEQ ID NO: 14 from amino acid 192 to amino acid 592;

(d) fragments of the amino acid sequence of SEQ ID NO:12 encoding a protein having mocarhagin activity; and

(e) the amino acid sequence encoded by the cDNA insert of clone NMM-13 deposited under accession number ATCC 209584;

the protein being substantially free from other mammalian proteins.

61. The composition of claim 60 wherein said protein comprises the amino acid sequence of SEQ ID NO:6.

67. A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:13 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

68. The protein of claim 67 comprising a mature protein.

69. A pharmaceutical composition comprising a protein of claim 60 and a pharmaceutically acceptable carrier.

70. A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 16;

(b) the amino acid sequence of SEQ ID NO: 16 from amino acid 62 to amino acid 462;

(c) fragments of the amino acid sequence of SEQ ID NO: 16 encoding a protein having mocarhagin activity; and

(d) the amino acid sequence encoded by the cDNA insert of clone NMM-3 deposited under accession number ATCC 209587;

the protein being substantially free from other mammalian proteins.

71. The composition of claim 70 wherein said protein comprises the amino acid sequence of SEQ ID NO:6.

77. A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:15 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

78. The protein of claim 77 comprising a mature protein.

79. A pharmaceutical composition comprising a protein of claim 70 and a pharmaceutically acceptable carrier.

80. A composition comprising a mocarhagin protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 18;

(b) the amino acid sequence of SEQ II) NO: 18 from amino acid 197 to amino acid 621;

(c) fragments of the amino acid sequence of SEQ ID NO:18 encoding a protein having mocarhagin activity; and

(d) the amino acid sequence encoded by the cDNA insert of clone NMM-9ek deposited under accession number ATCC 209583;

the protein being substantially free from other mammalian proteins.

81. The composition of claim 80 wherein said protein comprises the amino acid sequence of SEQ ID NO:6.

87. A protein produced according to a process comprising:

(a) in a suitable culture medium, growing a culture a host cell transformed with an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:17 operably linked to an expression control sequence; and

(b) purifying the protein from the culture.

88. The protein of claim 87 comprising a mature protein.

89. A pharmaceutical composition comprising a protein of claim 80 and a pharmaceutically acceptable carrier.

96. (New) A method of treating a condition characterized by P- or E-selectin mediated intercellular adhesion comprising administering a therapeutically effective amount of a composition of claim 7 to a mammalian subject.

97. (New) A method of treating a condition characterized by P- or E-selectin mediated intercellular adhesion comprising administering a therapeutically effective amount of a composition of claim 12 to a mammalian subject.

98. (New) The method of claims 96 or 97 wherein said condition characterized by P- or E-selectin mediated intercellular adhesion is selected from the group consisting of: myocardial infarction, vessel restenosis, thrombosis, bacterial or viral infection, metastatic conditions, inflammatory disorders such as arthritis, acute respiratory distress syndrome, asthma, emphysema, delayed type hypersensitivity reaction, systemic lupus erythmatosus, thermal injury, autoimmune thyroiditis, experimental allergic encephalomyelitis, multiple sclerosis, diabetes, Reynaud's syndrome, neutrophilic dermatosis, inflammatory bowel disease, Grave's disease, glomerulonephritis, gingivitis, periodontitis, hemolytic uremic syndrome, ulcerative colitis, Crohn's decease, necrotizing enterocoltis, granulocyte transfusion associated syndrome, and cytokine-induced toxicity.

99. (New) A method of treating a condition characterized by P- or E-selectin mediated intercellular adhesion comprising administering a therapeutically effective

amount of a composition of any one of claims 29, 39, 49, 59, 69, 79, or 89 to a mammalian subject.